Mathematical Modeling Lecture 9

Membrane currents and Hodgkin–Huxley gate kinetics

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Membrane charge balance

$$V = \phi_{\text{in}} - \phi_{\text{out}}, \qquad C\dot{V} = I_{\text{app}} - I_{\text{ion}}.$$

Applied current is positive inward; ionic current is positive outward.

Density and total current

$$[C] = \mu\mathrm{F/cm}^2, \quad [V] = \mathrm{mV}, \quad [t] = \mathrm{ms}.$$

$$\mu\mathrm{F} \cdot \mathrm{mV/ms} = \mu\mathrm{A}, \qquad I_{\mathrm{total}} = A_m I_{\mathrm{density}}.$$

Conductance and electrochemical driving difference

$$I_j = g_j(V - E_j).$$

A reversal potential makes one current zero, not necessarily the total current.

At $V < E_j$, this outward-positive current is negative.

The three conductance laws

$$g_{\mathrm{Na}} = 120 m^3 h, \quad g_{\mathrm{K}} = 36 n^4, \quad g_{\mathrm{L}} = 0.3.$$

$$(E_{\mathrm{Na}}, E_{\mathrm{K}}, E_{\mathrm{L}}) = (45, -82, -59)\,\mathrm{mV}.$$

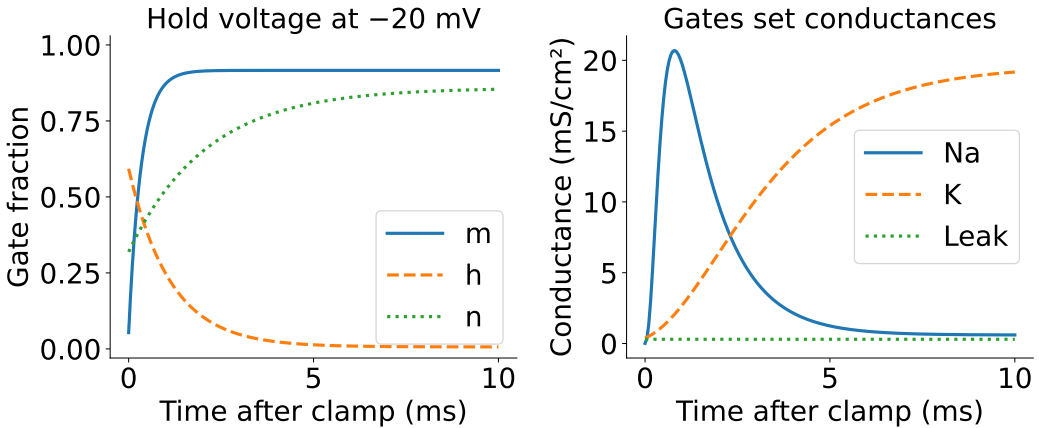
Conductances are in $\mathrm{mS/cm^2}$.

Gate opening and closing

$$\dot{s} = \alpha_s(V)(1 - s) - \beta_s(V)s, \qquad s \in \{m, h, n\}.$$

The source fractions enforce availability; rates are nonnegative and measured per millisecond.

Voltage-clamp relaxation



Voltage-clamp relaxation

$$s_\infty = \frac{\alpha}{\alpha + \beta}, \quad \tau_s = \frac{1}{\alpha + \beta}.$$

$$s(t) = s_\infty + (s_0 - s_\infty)e^{-t/\tau_s}.$$

A constant-rate gate calculation

$\alpha = 0.2$, $\beta = 0.8\,\mathrm{ms}^{-1}$, $s_0 = 0.9$:

$$s_\infty = 0.2, \quad \tau_s = 1\,\mathrm{ms}, \quad s(3) = 0.2 + 0.7e^{-3} \simeq 0.23485.$$

Activation rate functions

$$F(z) = \frac{z}{1 - e^{-z}}, \quad F(0) = 1.$$

$$\alpha_m = F((V + 45)/10), \qquad \beta_m = 4e^{-(V+70)/18},$$
$$\alpha_n = 0.1F((V + 60)/10), \quad \beta_n = 0.125e^{-(V+70)/80}.$$

Sodium availability rates

$$\alpha_h = 0.07e^{-(V+70)/20}, \qquad \beta_h = \frac{1}{1+e^{-(V+40)/10}}.$$

h is a gate variable, not the numerical time step.

Its loss during depolarization helps terminate sodium conduction.

Stable evaluation near a removable singularity

$$F(z) = 1 + \frac{z}{2} + \frac{z^2}{12} - \frac{z^4}{720} + O(z^6).$$

Use a local series near zero and $-\operatorname{expm1}(-z)$ elsewhere.

The physical rate remains finite at $V = -45, -60\,\mathrm{mV}$.

A self-consistent resting state

$$s = s_\infty(V_*), \qquad I_{\text{ion}}(V_*, s_\infty(V_*)) = 0.$$

The current parameter set gives $V_* \simeq -69.89767\,\text{mV}$.

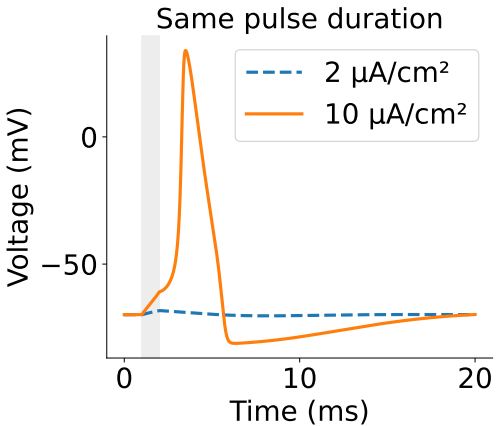
Regenerative and terminating feedback

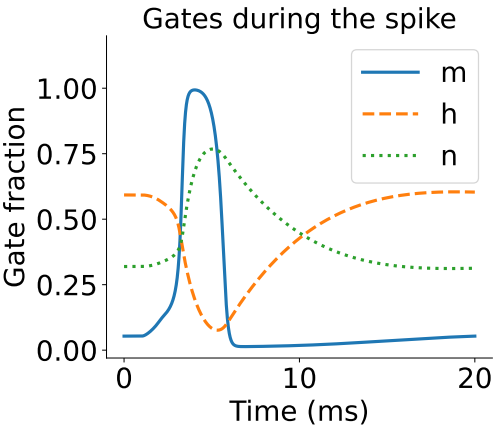
Depolarization increases sodium activation, which can increase inward current.

Sodium availability then falls; potassium conductance rises; driving differences also change.

Current is conductance times driving difference.

Current-driven pulse experiments





Current-driven pulse experiments

Pulse interval: $[1, 2)\,\mathrm{ms}$.
Amplitudes: 2 and $10\,\mu\mathrm{A}/\mathrm{cm}^2$.

A small excursion and a spike are two specified experiments, not a universal threshold measurement.

A signed ionic-current sum

At $V = -60\,\mathrm{mV}$, prescribe $g = (0.12, 0.36, 0.30)$:

$$I_{\mathrm{Na}} = -12.6, \quad I_{\mathrm{K}} = 7.92, \quad I_{\mathrm{L}} = -0.30.$$

$$I_{\mathrm{ion}} = -4.98\,\mu\mathrm{A}/\mathrm{cm}^2.$$

The voltage increment from current balance

$$\dot{V} = \frac{2 - (-4.98)}{1} = 6.98\,\mathrm{mV/ms}.$$

$$\Delta V \simeq 0.05(6.98) = 0.349\,\mathrm{mV}, \qquad V^{+} \simeq -59.651\,\mathrm{mV}.$$

An exact gate substep

Freeze $V = V^k$ during Δt:

$$s^{k+1} = s_\infty(V^k) + [s^k - s_\infty(V^k)]e^{-\Delta t/\tau_s(V^k)}.$$

This is a convex combination; no clipping is needed.

An exact frozen-conductance voltage substep

$$G = \sum_j g_j, \quad V_{\mathrm{tar}} = \frac{I_{\mathrm{app}} + \sum_j g_j E_j}{G}.$$

$$V^{k+1} = V_{\mathrm{tar}} + (V^k - V_{\mathrm{tar}}) e^{-G\Delta t/C}.$$

Event alignment and delivered charge

$$\int I_{\mathrm{app}}\,\mathrm{d}t = 10\,\mu\mathrm{A\,ms/cm^2}$$

for the 10-unit, one-millisecond pulse.

End a time step at each pulse edge; otherwise refinement can change the input itself.

Accuracy of the coupled membrane calculation

Exact substeps do not imply an exact coupled solution.

Check rest, gate bounds, rate limits, and common-time refinement.

The sequential split is generally first order in the full state; voltage alone may show higher apparent order in a specific experiment.